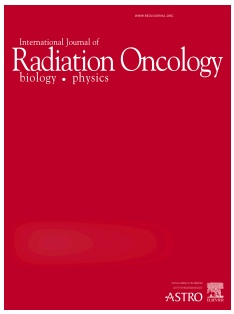
Eating As Treatment (EAT): A Stepped-Wedge, Randomized Controlled Trial of a Health Behavior Change Intervention Provided by Dietitians to Improve Nutrition in Patients With Head and Neck Cancer Undergoing Radiation Therapy (TROG 12.03)

Britton, Ben; Baker, Amanda L.; Wolfenden, Luke; Wratten, Chris; Bauer, Judith; Beck, Alison K.; McCarter, Kristen; Harrowfield, Jane; Isenring, Elizabeth; Tang, Colin; Oldmeadow, Chris; Carter, Gregory

Published in:
International Journal of Radiation Oncology Biology Physics

DOI:
10.1016/j.ijrobp.2018.09.027

Accepted Manuscript



Eating As Treatment (*EAT*): a stepped-wedge, randomised controlled trial of a health behaviour change intervention provided by dietitians to improve nutrition in patients with head and neck cancer undergoing radiotherapy (TROG 12.03)

Ben Britton, Amanda L. Baker, Luke Wolfenden, Chris Wratten, Judith Bauer, Alison K. Beck, Kristen McCarter, Jane Harrowfield, Elizabeth Isenring, Colin Tang, Chris Oldmeadow, Gregory Carter

PII: S0360-3016(18)33807-0

DOI: 10.1016/j.ijrobp.2018.09.027

Reference: ROB 25310

To appear in: *International Journal of Radiation Oncology • Biology • Physics*

Received Date: 14 November 2017

Revised Date: 14 September 2018

Accepted Date: 21 September 2018

Please cite this article as: Britton B, Baker AL, Wolfenden L, Wratten C, Bauer J, Beck AK, McCarter K, Harrowfield J, Isenring E, Tang C, Oldmeadow C, Carter G, *Eating As Treatment* (*EAT*): a stepped-wedge, randomised controlled trial of a health behaviour change intervention provided by dietitians to improve nutrition in patients with head and neck cancer undergoing radiotherapy (TROG 12.03), *International Journal of Radiation Oncology • Biology • Physics* (2018), doi: https://doi.org/10.1016/j.ijrobp.2018.09.027.

Eating As Treatment (*EAT*): a stepped-wedge, randomised controlled trial of a health behaviour change intervention provided by dietitians to improve nutrition in patients with head and neck cancer undergoing radiotherapy (TROG 12.03)

Ben Britton[1 2], Amanda L. Baker[1], Luke Wolfenden[1], Chris Wratten[3], Judith Bauer[4], Alison K. Beck[1], Kristen McCarter[5], Jane Harrowfield[6], Elizabeth Isenring[7], Colin Tang[8], Chris Oldmeadow[1 9], & Gregory Carter[1 2]

1 School of Medicine and Public Health, University of Newcastle, NSW, Australia
2 Psycho-Oncology Department, Calvary Mater Newcastle, NSW, Australia
3 Radiation Oncology Department, Calvary Mater Newcastle, NSW, Australia
4 Centre for Dietetics Research, The University of Queensland, QLD, Australia
5 School of Psychology, Faculty of Science & IT, University of Newcastle, NSW, Australia
6 Nutrition and Speech Pathology Department, Peter MacCallum Cancer Centre, VIC, Australia
7 Faculty of Health Sciences and Medicine, Bond University and Honorary Research Fellow, Princess Alexandra Hospital, QLD, Australia
8 Radiation Oncology, Sir Charles Gairdner Hospital, WA, Australia
9 CREDITSS—Clinical Research Design, Information Technology and Statistical Support Unit, Hunter Medical Research Institute

Corresponding Author
Ben Britton
Ben.britton@hnehealth.nsw.gov.au
Locked Bag 7
Hunter Region Mail Centre NSW 2310
Australia

Declaration of interests
We declare no competing interests.

Acknowledgements
Funding for the trial came from the National Health and Medical Research Council of Australia (APP1021018; 2011/ 3654). Coordinating ethics was granted by Hunter New England Health (HREC/12/HNE/108; HNEHREC: 12/04/18/4.06). Approval was also received from the following committees: Central Adelaide Local Health Network (HREC/13/RAH/75; SSA/13/RAH/102); Sir Charles Gairdner Group HREC (2012-136); Peter MacCallum Cancer Centre Ethics (SSA/13/ PMCC/19); Western Sydney Local Health District Research Governance (SSA/ 13/WMEAD/110); Metro South Hospital and Health Service (SSA/13/QPAH/ 240 and SSA/13/QPAH/241).

Title
Eating As Treatment (*EAT*): a stepped-wedge, randomised controlled trial of a health behaviour change intervention provided by dietitians to improve nutrition in patients with head and neck cancer undergoing radiotherapy

Running Title
Eating As Treatment in head & neck cancer

Abstract

Purpose
Malnutrition in head and neck cancer (HNC) treatment is common and associated with poorer morbidity and mortality outcomes. This trial aimed to improve nutritional status during radiotherapy using a novel method of training dietitians to deliver psychological techniques to improve HNC patients' nutritional behaviours.

Methods and Materials
This trial used a stepped wedge randomised controlled design to assess the efficacy of *Eating As Treatment* (*EAT*). Based on Motivational Interviewing and Cognitive Behavioural Therapy, *EAT* was designed to be delivered by oncology dietitians and integrated into their clinical practice. During control steps, dietitians provided treatment as usual, before being trained in *EAT* and moving into the intervention phase. The training was principles based and sought to improve behaviour change skills rather than provide specific scripts.

Patients recruited (151 controls, 156 intervention) to the trial were assessed at four time points (first and final week of Radiotherapy, four and twelve weeks post). The primary outcome was nutritional status at the end of RT as measured by the Patient Generated Subjective Global Assessment (PG-SGA).

Results
Patients who received the *EAT* intervention had significantly better scores on the primary outcome of nutritional status at the critical end of treatment time point (β=-1.53 (-2.93 to -.13) p=.03). Intervention patients were also significantly more likely to: be assessed as well-nourished at each time point; lose a smaller percentage of weight have fewer treatment interruptions; present lower depression scores; and report a higher quality of life. Although not statistically significant, those who received the intervention had fewer and shorter unplanned hospital admissions.

Conclusions
This trial is the first of its kind to demonstrate the effectiveness of a psychological intervention to improve nutrition in HNC patients receiving radiotherapy. It provides a means to ameliorate malnutrition and the important related outcomes and consequently should be incorporated into standard care for patients receiving HNC radiotherapy.

INTRODUCTION

Head and Neck Cancer (HNC) is the sixth most commonly diagnosed cancer worldwide[1]. Along with the rigours of treatment, HNC patients also face high rates of malnutrition[2]. Malnutrition while receiving cancer treatment is associated with increased morbidity[3] and reduced survival[4]. It is a common reason for treatment interruption[5], which reduces the effectiveness of radiotherapy (RT) and is strongly associated with increased mortality[6]. Therefore preventing malnutrition during RT is critical for improving both morbidity and mortality outcomes for HNC patients.

Dietitian support during RT demonstrably improves nutrition for HNC patients[7,8], however these interventions predominantly focus on dietetic advice rather than behavioural adherence. A recent comprehensive review of all nutritional interventions for HNC nutrition found no studies that focussed on patient behaviour change[8]. This is despite the strong evidence in other areas of health that behaviour change interventions and in particular cognitive behaviour therapy (CBT), are effective in improving nutrition[9].

The *EAT* trial builds on a promising pilot trial of a psychological intervention targeting behaviour, that found a significant benefit in survival over three years[10]. It is the first multi-centre randomised controlled trial of a psychological intervention to improve nutrition in HNC patients.

Aims and Hypotheses

The aim of this trial was to test the effectiveness of the *Eating As Treatment* (*EAT*) intervention. *EAT* is a dietitian-delivered intervention, designed to prevent malnutrition in patients with HNC undergoing RT.

It was hypothesised that patients with HNC receiving the *EAT* intervention would have better nutritional status scores, as measured by the Patient-Generated Subjective Global Assessment (PG-SGA), during their last week of RT, compared with patients in the control condition who received usual care.

Secondary hypotheses were that intervention patients would have benefits in other measures of nutrition, higher rates of treatment completion, fewer unplanned hospital admissions, shorter lengths of stay, lower depression scores, and higher quality of life.

METHODS AND MATERIALS

Detailed descriptions of the methods and intervention can be found in the published protocol[11] but are described briefly below.

Trial Design

The trial was a stepped wedge cluster randomised controlled trial (RCT). The stepped wedge was used because the nature of the intervention required the dietitians to acquire new skills, making contamination highly likely if they were then to provide a control condition in a RCT randomised at the level of the individual. The alternative therefore was to randomise at the hospital level, however a standard cluster randomised controlled trial required more hospitals seeing high numbers of HNC patients than were available within Australia. A stepped wedge randomised controlled trial provided the same level of evidence with fewer required clusters [12,13].

In a stepped wedge trial, all clusters begin in the control condition and then progress in a randomised order to the intervention condition (see supplementary Figure).

Site Recruitment

Six major Australian hospitals were recruited through the XXXXX. The only trial site eligibility criterion was that of treating a minimum of 100 HNC patients per year. The participating hospitals were from: XXXXX, South Australia; XXXXX, Victoria; XXXXX, Western Australia; XXXXX, New South Wales; and two hospitals in XXXXX, Queensland. The two hospitals in XXXXX shared a dietetic department. As such, while they were treated separately for analysis, they progressed to the intervention period at the same time, effectively reducing the number of intervention progression steps in the stepped wedge to five.

Randomisation

The order in which each site received the intervention was randomised by an independent statistician using a uniform random number generator in STATA[14].

Participants

Inclusion criteria

Patients eligible for inclusion met the following criteria: aged 18 years or older; pathologically confirmed diagnosis of HNC, that is, cancer involving the nasopharynx, oropharynx, oral cavity, larynx, or hypopharynx, requiring definitive or postoperative radiotherapy with curative intent (chemoradiation permitted including neoadjuvant and adjuvant chemotherapy); receiving regional nodal irradiation; receiving a prescribed dose of at least 60 Gy; available for follow-up for at least 6 months post study initiation; capacity to provide written informed consent.

Exclusion criteria

Criteria that made patients ineligible for inclusion were: inability to communicate in English; presence of organic brain diseases (impairing ability to complete questionnaires satisfactorily); likely insignificant oral or pharyngeal mucositis as a complication of radiotherapy treatment (patients with T1/T2 glottic carcinoma undergoing small-field radiotherapy or T1/T2 tonsil cancer undergoing unilateral treatment were excluded).

Treatment

Control

During the control phase, each hospital delivered treatment as usual, making no changes to any part of their clinical care.

Intervention

The "*Eating As Treatment*" intervention attempted to prevent malnutrition by reframing eating as part of a patient's RT treatment. To do this, oncology dietitians delivered *EAT* during their usual consultations with a weekly exposure while the patient was receiving RT, and then fortnightly thereafter. This frequency was in accordance with the national guidelines[15] and therefore was expected to be comparable to control phase session frequency.

EAT used CBT strategies and motivational interviewing (MI) consultation styles. These two approaches were distilled for specific use with HNC patients, who were struggling to maintain nutrition while receiving radiotherapy. The intervention was

successfully piloted by a clinical psychologist[10] and further refined for delivery by dietitians. Training in the intervention was tested on XXXXX oncology dietitians, who found the training acceptable and feasible[16].

EAT was designed to be a standardized but not highly manualised intervention. This approach is better integrated into existing clinical practices and less structured MI interventions have demonstrated significantly greater effect sizes than those that were highly manualised[17]. To achieve this, *EAT* was presented as a set of key principles and strategies (Figure 1) that could be implemented flexibly in different situations and contexts. Dietitians were trained in implementing these strategies regardless of dietetic advice or patient characteristics. *EAT* was designed to be delivered as part of existing practice, without requiring additional resources.

<Figure 1 about here>
Figure 1. Principles of *EAT* & *EAT* to LIVE

The first principle of *EAT* referred to the MI interactional style of a collaborative, empathic conversation[18] and guided the dietitians in constructing a conversation in which the patient reinforced their own reasons for change. Importantly it also avoided pushing the patient into creating arguments not to change, a common outcome of a clinician telling them what they should do.

Once motivation for good nutritional behaviour had been established, it was supported by CBT strategies aiming to reinforce the likelihood that the behaviour would happen after the patient had gone home. Principles 2,3 and 4 (Figure 1), underpin these strategies and were operationalized through a collaborative nutritional plan. At home the patient would work through their daily list of behaviours and tick off each item as it was completed. Through the nutrition planner the dietitian was able to utilize strategies of self-generation[18], self-monitoring[19], having a concrete plan[20], tailoring[21], achievability[22], and reinforcement and accountability[23]. Each of these strategies has been shown to be effective in changing nutritional behaviours in other populations.[9]

In week five of RT, when the patient's ability to eat was likely to have become impaired, dietitians conducted a nutritional assessment. This allowed them to discuss poor nutritional status in a non-confrontational way. Dietitians were then instructed to conduct the '*Eat to LIVE*' conversation (Figure 1.). Each element used MI to avoid patient defensiveness and the creation of arguments against change. The conversation established the patient's motivation to live; informed them of the poor outcomes associated with malnutrition; and subtly highlighted the variance between wanting to live and not performing nutritional behaviours that gave them the best chance of survival. This conversation required the dietitian to have the skill not to be confrontational or accusatory and relied heavily on the relationship they had built. Once the patient had articulated their motivation, the dietitian would then return to the other principles and strategies to translate this motivation into changes in dietary behaviours.

Variations to the *Eat to LIVE* conversation were allowed in two cases. In the first case, if the patient was performing all the behaviours the dietitians recommended, then there would be no variance to highlight and instead the dietitian deployed encouragement. Secondly, was when the dietitian found themselves having the *Eat to*

LIVE conversation earlier than week five of RT. This was allowed but dietitians were instructed to have the conversation again at week five.

Depression has been shown to be associated with malnutrition in HNC patients[24,25] and clinical depression may hinder the effectiveness of the *EAT* intervention by further reducing appetite and inhibiting the therapeutic relationship). To address this, dietitians were trained in how to administer the Patient Health Questionnaire-2 (PHQ-2)[26], a very brief depression screener derived from the first two items of the PHQ-9 described below. If the patient was screened as potentially depressed (PHQ-2 $\geq$3), the dietitian would notify their Radiation Oncologist and refer to whatever service their hospital had in place for psychological care.

Training

Dietitians received training in the *EAT* intervention as each site moved from the control to the intervention condition. Trainers, (clinical psychologists, behavioural researchers and dietitian) travelled to each hospital and provided an initial three days training which was supported by a 'booster' training session two months later. In addition, dietitians received regular telephone supervision to discuss cases and skills implementation with an *EAT* team clinical psychologist (XXXX).

Throughout both the control and the intervention periods, dietitians were required to audio record their sessions with study participants. A random sample of 20% of these recordings were then coded by study staff blinded to participant allocation as well as the content of the intervention. These recordings formed the basis of treatment fidelity, described in much greater detail in Beck et al (2015)[27].

To support the uptake and deployment of the *EAT* intervention the trial used several systems change strategies. These involved consulting multiple key hospital staff; academic detailing through shadowing days; systems changes such as ensuring the patient's RT was scheduled at a time when they could also see the dietitian; intervention performance, which was relayed back to managers; and provision of tools and resources such as stickers and water bottles prompting the *EAT* principles.

Outcomes

Outcome assessments were conducted by an independent researcher at four time points: first week of RT, last week of RT which was the primary endpoint, one-month post-RT, and three months post-RT.

Primary Outcome

The primary outcome of nutritional status at end of treatment was measured using the score (range= 1-49) of the Patient Generated Subjective Global Assessment scale (PG-SGA)[28]. The PG-SGA is considered the pre-eminent assessment in oncology nutrition[29] where a higher score is considered a worse nutritional status. The scale is comprised of both a self-report questionnaire and a clinical assessment conducted by the researcher. It incorporates known prognostic factors of nutrition including weight change, dietary intake, gastrointestinal symptoms, changes in functional capacity, nutritional intake, metabolic stress, subcutaneous fat, muscle wasting, disease and treatment.

Secondary outcomes

Nutritional Outcomes in addition to the scored PG-SGA were: the dietitian's Subjective Global Assessment (SGA) (A= Well Nourished, B= Moderately Malnourished and C= Severely Malnourished.); percentage weight loss; and weight loss >10%.

Depression was assessed using the validated Patient Health Questionnaire 9 (PHQ-9)[30]. Participants were asked to rate (on a scale of 0–3) the frequency of various Major Depressive Episode criteria over the previous 2 weeks. It measures the severity depression from 0 to 27.

Treatment interruptions and unplanned hospital admissions were extracted by chart review conducted by a local member of the study team as each patient completed the study. All other covariates (general demographics, tumour site, tumour stage, RT prescription, chemotherapy and surgery details) were collected in the same way.

Quality of Life (QOL) was assessed using the European Organisation for Research and Treatment of Cancer, Core Quality of Life Questionnaire (EORTC QLQ-C30). This is a validated[31] 30-item self-report questionnaire designed to measure quality of life in patients with cancer. The questionnaire consists of five functional scales (physical, role, cognitive, emotional and social), three symptom scales (fatigue, pain, nausea and vomiting), a global health status scale, and six single items assessing the perceived financial impact of the disease and additional symptoms commonly reported by patients with cancer (dyspnoea, loss of appetite, insomnia, constipation and diarrhoea).

Sample Size

A sample size calculation found that 400 participants would provide 80% probability that the study would detect a difference between intervention and control periods at a two-sided .05 significance level. There were no published minimum clinically important differences for the PG-SGA, so the calculation used estimates from the pilot trial which found a significant difference in mortality was associated with a 2 point change in the PG-SGA and a standard deviation of 7[10].

Blinding

All efforts were made to blind the outcome assessors to the intervention content and delivery. However, because the assessments took place in the participating hospitals, it was not possible to guarantee that the assessors were blind to intervention delivery via awareness that training had taken place. Due to the nature of the intervention it was not possible to blind the dietitians providing the intervention. Participants were blinded to treatment allocation.

Statistical Methods

All analyses were carried out using STATA 13[32]. The primary outcome of nutritional status as measured by the PG-SGA was analysed using an intention to treat, Linear Mixed Models (LMM) regression. The assumptions of the linear mixed models were assessed by inspecting appropriate residual plots. The model, nominated in the protocol [33], used an unstructured covariance and included the following:

Cluster level variables of intervention period to test the effectiveness of the *EAT* intervention, and hospital cluster; to adjust for differences between hospitals; Individual level variables of baseline PG-SGA, to adjust for differences in baseline

nutrition and improve the power to detect a difference; calendar time, to adjust for any background temporal effects that could have confounded the stepped-wedge design; assessment moment; to adjust for differences in nutrition throughout RT and recovery; and Tumour site and stage, to adjust for any differences between groups' nutritional status due to differences in malignancies. The model also included an interaction between intervention and assessment moment to allow the treatment effect to vary over RT time and compare the intervention effect at the end of treatment. The model included a random individual level intercept to account for the repeated measures on individuals over assessment moments, and a random coefficient for assessment moment to allow for heterogeneity in subject specific trends.

Secondary outcomes were assessed using the same model without the interaction term to analyse the average across all time points. Percentage weight loss, depression (PHQ-9) and QOL (QLQ C30) were analysed using LMM while the categorical dietitians' subjective global assessment of nutritional status (SGA) and >10% weight loss were analysed using logistic mixed effects models.

Treatment interruption was analysed using a logistic regression. Unplanned hospital admissions were analysed using a negative binomial regression. Both models included intervention period, baseline nutritional status, hospital and calendar time.

Findings

Between July 2013 and January 2016, 307 participants were recruited with the final follow-up assessment conducted in May 2016 (Figure 2). One of the six hospitals failed to recruit any patients and withdrew within the first 9 months, leaving 5 hospitals across 4 intervention sites. Baseline characteristics for the control and the intervention periods are presented in Table 1 and suggest that periods were comparable.

<Figure 2 about here>
Figure 2. Consort diagram

Fidelity
Blind fidelity ratings of the session tapes yielded very high inter- and intra-rater reliability and showed that dietitians delivered the intervention satisfactorily to pre-specified levels[34]. The Eat To Live conversation was utilised outside of week 5 in 14% of the sampled on-radiotherapy session recordings[34].

<Table 1 about here>

Primary Outcome
Nutritional status as measured by the PG-SGA, found that participants in the intervention group had significantly lower (better) scores than those in the control group at the end of RT (β=-1.53 CI -2.93 to -.13 p=.03) (Table 2). A breakdown of the components of the PG-SGA is presented in Figure 3.

<Table 2 about here>

<Figure 3 about here>

Figure 3. Mean PG-SGA Parts A, B, C & D across all time points, overlayed with 95% CI of the model margins comparing intervention and controls

Secondary Outcomes (Table 2)
Nutritional Outcomes
Those in the intervention group were significantly more likely to be in the Subjective Global Assessment (SGA) category A: Well-nourished or anabolic across all follow up time points.

Almost all participants lost weight from baseline (304 of the 307) and the LMM regression showed controls lost a significantly higher percentage of their baseline weight. Significantly more control participants experienced more than 10% weight loss.

Depression
Patients in the intervention group had significantly lower depression scores than those in the control group.

Treatment Interruptions
Twenty-one controls (14%) experienced RT treatment interruptions compared to 12 (8%) in the intervention, a difference that was statistically significant.

Unplanned Hospital Admissions
Those in the control condition had more unplanned hospital admissions than those in the intervention for a greater number of total days, and a greater average length of stay. However, none of these differences were statistically significant.

Quality of Life
The summary scale of the QLQ C30 showed that intervention patients had significantly better overall QOL than those in the control condition. This difference appears to be a result of the significant differences in nausea and vomiting, appetite loss, physical and cognitive functioning (Table 3).

<Table 3 about here>

DISCUSSION
The EAT intervention demonstrated superior nutritional status scores compared to controls as measured by the PG-SGA at the critical time point at the end of RT. Following RT, the nutritional status of all patients improved, suggesting that patients resumed their usual eating and drinking as RT side effects subsided. These findings indicate that a behavioural intervention conducted during RT reduces eating difficulties, and supports the nutritional guidelines[15] that long-term nutritional intervention is not necessary for most patients.

Averaged across all time periods, intervention patients were more likely to be categorised as well nourished (SGA category A), lost a lower percentage of their body weight and were less likely to lose >10% of their baseline weight. These results all indicate that the *EAT* intervention was an effective method of improving or maintaining nutritional status in HNC patients receiving RT.

Intervention patients had significantly fewer RT interruptions. These secondary findings are important because they are a possible mechanism explaining the association between malnutrition and reduced survival found in previous studies.

In addition to reducing nutritional decline and improving nutrition related outcomes, the *EAT* intervention, which included training the dietitians in a simple depression screen and referral where indicated, showed a reduction in depression scores on the PHQ-9. Without adding any new services or time to the dietetic consult, the timely referral to whatever service was available locally resulted in significantly reduced depressive symptoms in HNC patients undergoing RT. This reinforces the current recommendations that dietitians should be screening for depression[15].

A potential criticism of the study is that despite being significant, the difference in PG-SGA score was small (β =-1.53). Because there are no published minimum important differences for the PG-SGA, alternative assessments of the meaningfulness of the effect are necessary. Some context of the size of the difference can be gained by comparing the intervention parameter estimate to that of other variables in the linear mixed model. The improvement on PG-SGA score for *EAT* was seven times greater than that of the most common dietetic intervention of feeding tube insertion (β =-.21 SE±.64). In fact, the intervention effect on PG-SGA was only smaller than the non-modifiable factors of hospital and cancer type. The clinical significance of EAT is further supported by the difference in PG-SGA scores being associated with improvements in other clinically meaningful outcomes such as the dieticians' Subjective Global Assessment of nutritional status, and overall quality of life scores using the EORTC QLQ-C30.

A second limitation of the study was the potential for assessor bias. Although they were not part of the intervention, it was not possible to guarantee that the outcome assessors in the hospitals were unaware of the treatment period. Nevertheless the overall intervention effect remains even when the subjective physical exam component of the PG-SGA was removed from the analysis.

Strengths of the study are the very high ecological validity, being provided by practising clinicians in working Australian radiation oncology units. The ongoing cost of the intervention was very low, not requiring any additional physical or personnel resources and being integrated into existing dietetic sessions.

Further research is underway in long-term follow up of mortality, intervention acceptability, cost effectiveness and examination of the efficacy of the different intervention elements.

This trial is the first of its kind internationally to demonstrate significant and clinically meaningful benefits of psychological strategies, delivered by dietitians, to improve malnutrition in HNC patients. Intervention participants exhibited better nutrition, less weight loss, lower depression scores, fewer RT interruptions and better QOL scores. The *EAT* intervention is an effective and achievable intervention that has shown improvement in a multi-centre trial around Australia. It should be considered for use in all RT departments in which malnutrition in HNC patients is a problem.

References:

1. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. [Internet]. 2nd ed. Lyon, France: International Agency for Research on Cancer; 2015 [cited 2017 Jan 28]. Available from: http://globocan.iarc.fr/

2. Capuano G, Gentile PC, Bianciardi F, Tosti M, Palladino A, Di Palma M. Prevalence and influence of malnutrition on quality of life and performance status in patients with locally advanced head and neck cancer before treatment. Support Care Cancer. 3rd ed. Springer-Verlag; 2010 Apr;18(4):433–7.

3. Larsson M, Hedelin B, Johansson I, Athlin E. Eating problems and weight loss for patients with head and neck cancer: a chart review from diagnosis until one year after treatment. Cancer Nursing. 2005;28(6):425–5.

4. van Leeuwen PA, Kuik DJ, Klop WM, Sauerwein HP, Snow GB, Quak JJ, et al. The impact of nutritional status on the prognoses of patients with advanced head and neck cancer. Cancer. 1999;86(3):519–27.

5. O'Connor P. The impact of missed fractions in head and neck radiotherapy and how they can be minimised. Radiography. 2013 Aug;19(4):343–6.

6. Fesinmeyer MD, Mehta V, Blough D, Tock L, Ramsey SD. Effect of Radiotherapy Interruptions on Survival in Medicare Enrollees With Local and Regional Head-and-Neck Cancer. International Journal of Radiation Oncology*Biology*Physics. 2010 Nov;78(3):675–81.

7. Isenring EA, Capra S, Bauer JD. Nutrition intervention is beneficial in oncology outpatients receiving radiotherapy to the gastrointestinal or head and neck area. British journal of cancer. 2004;91(3):447–52.

8. Langius JAE, Zandbergen MC, Eerenstein SEJ, van Tulder MW, Leemans CR, Kramer MHH, et al. Effect of nutritional interventions on nutritional status, quality of life and mortality in patients with head and neck cancer receiving (chemo)radiotherapy: a systematic review. Clin Nutr. 2013 Oct;32(5):671–8.

9. Spahn JM, Reeves RS, Keim KS, Laquatra I. State of the Evidence Regarding Behavior Change Theories and Strategies in Nutrition Counseling to Facilitate Health and Food Behavior Change. Journal of the American Dietetic Association. 2010;10(6):879–91.

10. Britton B, Baker A, Clover K, McElduff P, Wratten C, Carter G. Heads Up: a pilot trial of a psychological intervention to improve nutrition in head and neck cancer patients undergoing radiotherapy. European journal of cancer care. 2016 Apr 28;26(4).

11. Britton B, McCarter K, Baker A, Wolfenden L, Wratten C, Bauer J, et al. Eating As Treatment (EAT) study protocol: a stepped-wedge, randomised controlled trial of a health behaviour change intervention provided by dietitians to improve nutrition in patients with head and neck cancer undergoing radiotherapy. BMJ Open. 2015 Jul 31;5(7):e008921–12.

12. Hussey MA, Hughes JP. Design and analysis of stepped wedge cluster randomized trials. Contemporary Clinical Trials. 2007 Feb;28(2):182–91.

13. Hemming K, Haines TP, Chilton PJ, Girling AJ, Lilford RJ. The stepped wedge cluster randomised trial: rationale, design, analysis, and reporting. BMJ. 2015 Feb 6;350:h391.

14. StataCorp. *Stata Statistical Software: Release 11*. College Station, TX: StataCorp LP; 2009.

15. Findlay M, Bauer J, Brown T, Head and Neck Guideline Steering Committee. In: Head and Neck Guideline Steering Committee. Evidence-based practice guidelines for the nutritional management of adult patients with head and neck cancer. [Internet]. URL httpwiki.cancer.org.auaustraliawikiindex.phpoldid. Sydney; 2014 [cited 2014 Sep 10]. pp. 1–10. Available from: http://wiki.cancer.org.au/australia/COSA:Head_and_neck_cancer_nutrition_guidelines.

16. Beck AK, Britton B, Baker A, Wratten C, Odelli C, Bauer J, et al. Preliminary report: training head and neck cancer dietitians in behaviour change counselling. Psycho-oncology. 2016 Apr 6;26(3):405–7.

17. Hettema J, Steele J, Miller WR. Motivational interviewing. Annu Rev Clin Psychol. 2005;1(1):91–111.

18. Miller WR, Rollnick S. Motivational Interviewing, Third Edition. New York: Guilford Publication; 2012. 1 p.

19. Tate DF, Jackvony EH, Wing RR. Effects of Internet Behavioral Counseling on Weight Loss in Adults at Risk for Type 2 Diabetes: A Randomized Trial. Jama The Journal Of The American Medical Association. American Medical Association; 2003 Apr 9;289(14):1833–6.

20. Wing R, Jeffrey R, Burton L, Thorson C, Nissinoff K, Baxter J. Food provision vs structured meal plans in the behavioral treatment of obesity. Int J Obes Relat Metab Disord. 1996 Jan 1;20(1):56–62.

21. Clark M, Hampson SE, Avery L, Simpson R. Effects of a tailored lifestyle self-management intervention in patients with Type 2 diabetes. British Journal of Health Psychology. Blackwell Publishing Ltd; 2004 Sep 1;9(3):365–79.

22. Bandura A. Self-efficacy: toward a unifying theory of behavioral change. 1977 Mar;84(2):191–215.

23. Beck JS. Cognitive Behavior Therapy, Second Edition. Guilford Press; 2011. 1 p.

24. Kim S-A, Roh J-L, Lee S-A, Lee S-W, Kim S-B, Choi S-H, et al. Pretreatment depression as a prognostic indicator of survival and nutritional status in patients with head and neck cancer. Cancer. 2015 Sep 15;122(1):131–40.

25. Britton B, Clover K, Bateman L, Odelli C, Wenham K, Zeman A, et al. Baseline depression predicts malnutrition in head and neck cancer patients undergoing radiotherapy. Support Care Cancer. 2011 Jan 14;20(2):335–42.

26. Löwe B, Kroenke K, Gräfe K. Detecting and monitoring depression with a two-item questionnaire (PHQ-2). Journal of psychosomatic research. 2005 Feb;58(2):163–71.

27. Beck AK, Baker A, Britton B, Wratten C, Bauer J, Wolfenden L, et al. Fidelity considerations in translational research: Eating As Treatment - a stepped wedge, randomised controlled trial of a dietitian delivered behaviour change counselling intervention for head and neck cancer patients undergoing radiotherapy. Trials. 2015 Oct 15;16:465.

28. Ottery FD. Definition of standardized nutritional assessment and interventional pathways in oncology. Nutrition (Burbank, Los Angeles County, Calif). 1996;12(1 Suppl):S15–9.

29. Jager-Wittenaar H, Ottery FD. Assessing nutritional status in cancer. Current Opinion in Clinical Nutrition and Metabolic Care. 2017 Sep;20(5):322–9.

30. Kroenke K, Kroenke K, Spitzer RL, Spitzer RL, Williams JB, Williams JB. The PHQ-9: validity of a brief depression severity measure. J Gen Intern Med [Internet]. 2001 Sep;16(9):606–13. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1495268\&tool=pmcentrez\&rendertype=abstract

31. King M, Costa D, Aaronson NK, Brazier J, Cella DF, Fayers P, et al. PCN98 The Development of an Internationally-Valid Cancer-Specific Multi-Attribute Utility Instrument (MAUI) From the Eortc Core Health-Related Quality of Life (HRQOL) Questionnaire, QLQ-C30. Value in Health. Elsevier; 2012;15(4):A225.

32. StataCorp. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP; 2013.

33. Britton B, McCarter K, Baker A, Wolfenden L, Wratten C, Bauer J, et al. Eating As Treatment (EAT) study protocol: a stepped-wedge, randomised controlled trial of a health behaviour change intervention provided by dietitians to improve nutrition in patients with head and neck cancer undergoing radiotherapy. BMJ Open. 2015 Jul 31;5(7):e008921–12.

34. Beck AK, Britton B, Baker A, Wratten C, Bauer J, Wolfenden L, et al. “EAT”: Eating As Treatment. Training Head and Neck Cancer Dietitians in a Health Behaviour Change Intervention. Psycho-oncology. 2017 May p. InPress.

Figure 1. Principles of *EAT* & *EAT* to LIVE

Figure 2. Consort diagram

Figure 3. PG-SGA Parts A, B, C & D across all time points, overlayed with 95% CI of the baseline-adjusted model margins comparing intervention and controls

Table 1. Baseline Participant Characteristics

Variable	Control n(%)	Intervention n(%)
Male	126 (83)	118 (76)
Aboriginal or Torres Strait Islander	3 (2)	3 (2)
Non-English speaker at home	11 (7)	11 (7)
Marital Status		
Married/Defacto	102 (68)	91 (59)
Separated/Divorced/Widowed	32(21)	37 24)
Single never married	17 (11)	23 (15)
Highest level of education		
Primary School	2 (1)	2 (1)
High School	72 (47)	83 (53)
University/Vocational College	76 (51)	70 (45)
Other	1 (1)	0 (0)
Depression (PHQ-9)		
Minimal	98 (67)	98 (64)
Mild to Moderate	39 (27)	51 (34)
Moderately Severe to Severe	9 (6)	3 (2)
Tumour site		
Nasopharynx	12 (8)	11 (7)
Oropharynx	83 (55)	88 (56)
Oral Cavity	30 (20)	36 (23)
Larynx	14 (9)	15 (10)
Hypopharynx	9 (6)	2 (1)
Unknown Primary	3 (2)	4 (3)
Tumour stage		
I	6 (4)	6 (4)
II	22 (15)	17 (11)
III	25 (17)	32 (20)
IV	98 (65)	101 (65)
Dysphagia rating (CTCAE)		
Absent	98(66)	108(69)
Symptomatic, able to eat	27(18)	20(13)
Symptomatic, altered eating	16(11)	20(13)
Severely altered eating	8(5)	8(5)
Life threatening	0(0)	0(0)
Concurrent Chemotherapy	121 (80)	126 (82)
Platinum-based	101 (67)	104 (67)
Cetuximab	19 (13)	21 (21)

Post-Operative Radiotherapy	44 (29)	53 (34)
Prophylactic PEG	33 (22)	38 (25)
Prophylactic NGT	3 (2)	4 (3)
Continuous Variables	Mean(SD)	Mean(SD)
Age	58 (10)	58 (11)
Prescribed Radiation (Gy)	68 (4)	68 (3)
Fraction number	34 (2)	34 (2)
Nutritional Status (PG-SGA)	5 (5)	5 (5)

Table 2. Comparisons of Primary and Secondary Outcomes

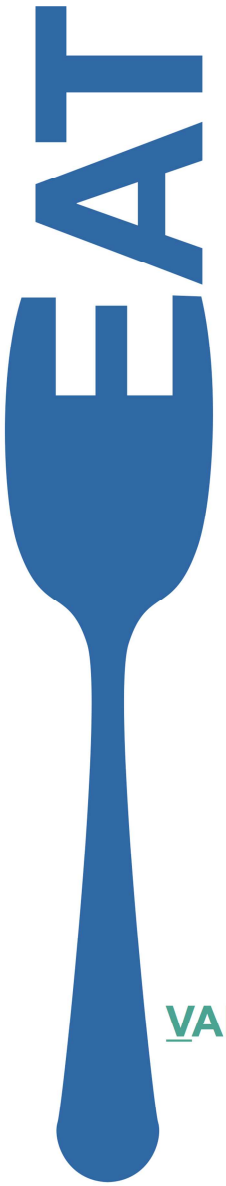
Outcome		Means, % or Counts		Statistic	(95% CI)		p
		Control	Intervention				
Primary Outcome							
PG-SGA +	Last wk	16.24	14.71	β=-1.53	(-2.93	-.13)	.03
Secondary Outcomes							
SGA category A*	1st wk	87%	84%	OR=2.88	(1.38	5.99)	<.01
	Last wk	21%	34%				
	1 mth	43%	49%				
	3 mth	69%	71%				
>10% weight loss	Last wk	37%	24%	OR=.23	(.06	.86)	.03
	1 mth	55%	39%				
	3 mth	63%	49%				
Percentage Weight loss		9.88	8.64	β=-1.24	(-2.35	-.13)	.03
PHQ-9 depression score		6.68	5.79	β=-.88	(-1.74	-.02)	.04
RT interruptions		14%	8%	OR=.23	(.06	.92)	.04
Unplanned admissions		130	100	IRR=.73	(.52	1.03)	.07
Mean length of stay		6.1	4.1	β=-1.80	(-4.09	.50)	.13
Total days		922	653				

+Higher score indicates worse nutritional status/risk

*SGA A = well nourished B= moderately malnourished C= severely malnourished

Table 3. Intervention vs Control in LMM of mean Health Related Quality of Life (QLQ C30) across End of Treatment, 1 Month Post RT & 3 Months Post RT

Category	Scale	β	(95% CI)		p
Total HRQOL score		.45	(.35	.54)	<.01
Global Health (higher is better)	Global Health Status	.97	(-2.53	4.48)	.57
Functioning Scales (higher is better)	Role functioning	3.76	(-1.54	9.06)	.16
	Physical Functioning	4.60	(1.07	8.13)	.01
	Emotional Functioning	3.31	(-.06	6.68)	.05
	Cognitive Functioning	5.34	(1.47	9.12)	<.01
	Social Functioning	2.93	(-1.87	7.35)	.23
Symptom Scales (lower is better)	Fatigue	-3.30	(-7.60	1.01)	.13
	Nausea & Vomiting	-7.12	(-10.85	-3.37)	<.01
	Pain	.83	(-3.85	5.51)	.73
	Dyspnoea	-3.43	(-7.14	.28)	.07
	Insomnia	.27	(-4.96	5.49)	.91
	Appetite Loss	-7.18	(-13.35	1.01)	.02
	Constipation	-2.01	(-6.21	2.18)	.35
	Diarrhoea	-1.03	(-4.08	2.03)	.51
	Financial Difficulties	-2.03	(-7.32	3.26)	.45



Eating as Treatment

PRINCIPLES OF BEHAVIOUR CHANGE

People are more likely to carry out a particular behaviour if:

1. they argue for the behaviour themselves
2. it is part of a concrete plan they devise themselves
3. it is recorded externally
4. they feel it is important, achievable and is being *monitored*

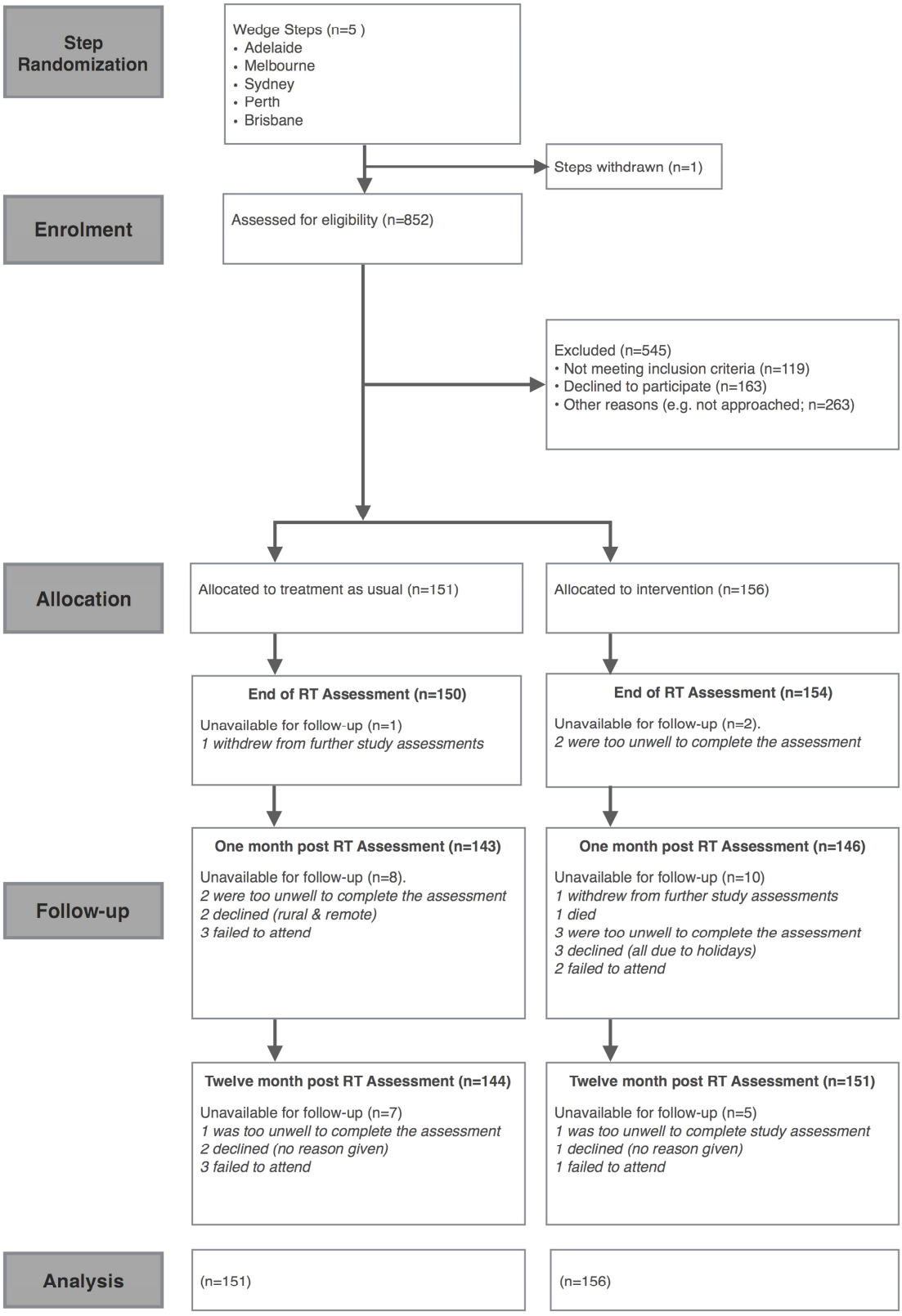
EAT TO LIVE

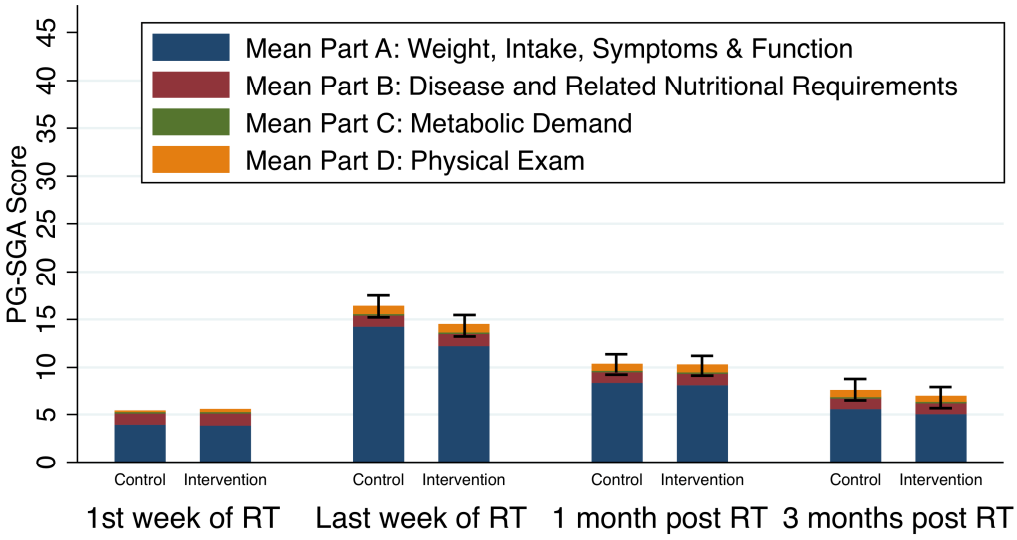
LIVING Why are you having radiotherapy?

INVITE I wonder if I can tell you something about malnutrition during treatment?

VARIANCE I'm puzzled by the difference between what you want and what you are currently doing with your nutrition

ELICIT What's the next step?


Step Randomization
Wedge Steps (n=5)
• Adelaide
• Melbourne
• Sydney
• Perth
• Brisbane
Steps withdrawn (n=1)
Enrolment
Assessed for eligibility (n=852)
Excluded (n=545)
• Not meeting inclusion criteria (n=119)
• Declined to participate (n=163)
• Other reasons (e.g. not approached; n=263)
Allocation
Allocated to treatment as usual (n=151)
Allocated to intervention (n=156)
End of RT Assessment (n=150)
Unavailable for follow-up (n=1)
1 withdrew from further study assessments
End of RT Assessment (n=154)
Unavailable for follow-up (n=2).
2 were too unwell to complete the assessment
Follow-up
One month post RT Assessment (n=143)
Unavailable for follow-up (n=8).
2 were too unwell to complete the assessment
2 declined (rural & remote)
3 failed to attend
One month post RT Assessment (n=146)
Unavailable for follow-up (n=10)
1 withdrew from further study assessments
1 died
3 were too unwell to complete the assessment
3 declined (all due to holidays)
2 failed to attend
Twelve month post RT Assessment (n=144)
Unavailable for follow-up (n=7)
1 was too unwell to complete the assessment
2 declined (no reason given)
3 failed to attend
Twelve month post RT Assessment (n=151)
Unavailable for follow-up (n=5)
1 was too unwell to complete study assessment
1 declined (no reason given)
1 failed to attend
Analysis
(n=151)
(n=156)



Summary
Malnutrition during head and neck cancer is associated with poorer morbidity and mortality outcomes. This trial assessed the effectiveness of a psychological intervention delivered by dietitians to prevent malnutrition in head and neck cancer patients while having radiotherapy. Those patients that received the intervention had significantly better nutritional scores; lost less weight; had fewer radiotherapy interruptions; had lower depression scores; and reported a higher quality of life.